

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

#### 21 CFR Part 862

[Docket No. 2004P–0354]

### Medical Devices; Clinical Chemistry and Clinical Toxicology Devices; Classification of Sirolimus Test System Devices

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Final rule.

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**SUMMARY:** The Food and Drug Administration (FDA) is classifying the sirolimus test system device into class II (special controls). The special control that will apply to the device is the guidance document entitled “Class II Special Controls Guidance Document: Sirolimus Test Systems.” The device is intended to measure sirolimus levels in whole blood as an aid to managing therapy for transplant patients receiving sirolimus, an immunosuppressive drug. The agency is classifying the device into class II (special controls) in order to provide a reasonable assurance of safety and effectiveness of the device. Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice of availability of a guidance document that is the special control for this device.

**DATES:** This rule becomes effective [*insert date 30 days after date of publication in the Federal Register*]. The classification was effective July 28, 2004.

**FOR FURTHER INFORMATION CONTACT:** Avis Danishefsky, Center for Devices and Radiological Health (HFZ–440), Food and Drug Administration, 2098 Gaither Rd., Rockville, MD 20850, 301–594–1243, ext. 161.

**SUPPLEMENTARY INFORMATION:****I. Background**

In accordance with section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360c(f)(1)), devices that were not in commercial distribution before May 28, 1976, the date of enactment of the Medical Device Amendments of 1976 (the amendments), generally referred to as postamendments devices, are classified automatically by statute into class III without any FDA rulemaking process. These devices remain in class III until the device is classified or reclassified into class I or II, or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the act, to a predicate device. The agency determines whether new devices are substantially equivalent to previously marketed devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807) of FDA's regulations.

Section 513(f)(2) of the act provides that any person who submits a premarket notification under section 510(k) of the act for a device that has not previously been classified may, within 30 days after receiving an order classifying the device in class III under section 513(f)(1) of the act, request FDA to classify the device under the criteria set forth in section 513(a)(1) of the act. FDA shall, within 60 days of receiving such a request, classify the device by written order. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a document in the **Federal Register** announcing such classification (section 513(f)(2) of the act).

In accordance with section 513(f)(1) of the act, FDA issued a document on June 15, 2004, classifying the Microgenics CEDIA Sirolimus Assay in class

III because it was not substantially equivalent to a device that was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, or a device which was subsequently reclassified into class I or class II. On June 16, 2004, Microgenics Corp. submitted a petition requesting classification of the Microgenics CEDIA Sirolimus Assay under section 513(f)(2) of the act. The manufacturer recommended that the device be classified into class II.

In accordance with 513(f)(2) of the act, FDA reviewed the petition in order to classify the device under the criteria for classification set forth in 513(a)(1) of the act. Devices are to be classified into class II if general controls, by themselves, are insufficient to provide reasonable assurance of safety and effectiveness, but there is sufficient information to establish special controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the petition, FDA determined that the Microgenics CEDIA Sirolimus Assay can be classified in class II with the establishment of special controls. FDA believes these special controls, in addition to general controls, will provide reasonable assurance of safety and effectiveness of the device.

The device is assigned the generic name sirolimus test system and is identified as a device intended to quantitatively determine sirolimus concentrations in whole blood. Measurements are used as an aid in management of transplant patients receiving therapy with sirolimus.

FDA has identified no direct risks to health related to use of sirolimus test systems. However, FDA has identified improper patient management, which involves failure of the test to perform as indicated or error in interpretation of results, as an indirect risk to health related to use of this

device. For example, a falsely low sirolimus measurement could contribute to a decision to raise the sirolimus dose above that which is necessary for therapeutic benefit. This could result in increased risk in the form of thrombocytopenia, leukopenia, anemia, or hyperlipidemia. A falsely high sirolimus measurement could contribute to a decision to decrease the dose below that which is necessary for immunosuppression. This could result in increased risk of rejection of the transplanted organ. Since optimal ranges for sirolimus may vary depending on the metabolite cross-reactivity of the specific assay, as well as on clinical factors, use of assay results to adjust a treatment regimen without consideration of such factors could also lead to improper patient management. Therefore, in addition to the general controls of the act, the device is subject to special controls, identified as the guidance document entitled “Class II Special Controls Guidance Document: Sirolimus Test Systems.”

The class II special controls guidance document also provides information on how to meet premarket (510(k)) submission requirements for the device, including recommendations on validation of performance characteristics and labeling. FDA believes that following the class II special controls guidance document generally addresses the risks to health identified in the previous paragraph. Therefore, on July 28, 2004, FDA issued an order to the petitioner classifying the device into class II. FDA is codifying this classification by adding 21 CFR 862.3840.

Following the effective date of this final classification rule, any firm submitting a 510(k) premarket notification for a sirolimus test system will need to address the issues covered in the special controls guidance. However, the firm need only show that its device meets the recommendations of the

guidance or in some other way provides equivalent assurance of safety and effectiveness.

Section 510(m) of the act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. For this type of device, FDA has determined that premarket notification is necessary to provide reasonable assurance of safety and effectiveness. FDA review of performance characteristics, test methodology, and labeling to satisfy requirements of § 807.87(e), will provide reasonable assurance that acceptable levels of performance for both safety and effectiveness will be addressed before marketing clearance. Thus, persons who intend to market this type of device must submit to FDA a premarket notification containing information on the sirolimus test system they intend to market, before marketing the device.

## **II. Environmental Impact**

The agency has determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

## **III. Analysis of Impacts**

FDA has examined the impacts of the final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and

equity). The agency believes that this final rule is not a significant regulatory action under the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because classification of these devices into class II will relieve manufacturers of the device of the cost of complying with the premarket approval requirements of section 515 of the act (21 U.S.C. 360e), and may permit small potential competitors to enter the marketplace by lowering their costs, the agency certifies that the final rule will not have a significant impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing “any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year.” The current threshold after adjustment for inflation is \$110 million. FDA does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

#### **IV. Federalism**

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency has concluded that the rule does not contain policies that have federalism implications as defined in the Executive

order and, consequently, a federalism summary impact statement is not required.

## **V. Paperwork Reduction Act of 1995**

This final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

## **VI. Reference**

The following reference has been placed on display in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Petition from Microgenics Corp., dated June 16, 2004.

## **List of Subjects in 21 CFR Part 862**

Medical devices.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 862 is amended as follows:

### **PART 862—CLINICAL CHEMISTRY AND CLINICAL TOXICOLOGY DEVICES**

■ 1. The authority citation for 21 CFR part 862 continues to read as follows:

**Authority:** 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

■ 2. Section 862.3840 is added to subpart D to read as follows:

#### **§ 862.3840 Sirolimus test system.**

(a) *Identification.* A sirolimus test system is a device intended to quantitatively determine sirolimus concentrations in whole blood.

Measurements are used as an aid in management of transplant patients receiving therapy with sirolimus.

(b) *Classification*. Class II (special controls). The special control is FDA's guidance document entitled "Class II Special Controls Guidance Document: Sirolimus Test Systems." See § 862.1(d) for the availability of this guidance document.



Dated: September 21, 2004.

**Linda S. Kahan,**

*Deputy Director, Center for Devices and Radiological Health.*

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